Citation:

Cross AJ, Peters U, Kirsh VA, Andriole GL, Reding D, Hayes RB, Sinha R. A prospective study of meat and meat mutagens and prostate cancer risk. *Cancer Res* 2005; 65: 11779-11784.

PubMed ID: 16357191

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to investigate whether meat intake or meat-related mutagens was associated with an increased risk for prostate cancer.

Inclusion Criteria:

Participants were included if participating in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

Exclusion Criteria:

Exclusion criteria included the following:

- history of cancer (other than nonmelanoma skin cancer);
- did not have prostate cancer screening results;
- lacked any of the following three questionnaires annual follow-up, baseline risk factor, or food frequency questionnaire (FFQ);
- missed more than seven items on the FFQ; or
- were extreme outliers for reported energy intake.

Description of Study Protocol:

Recruitment

Participants were selected from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.

Design

Between 1993 and 2001, men aged 55-74 years were randomized to the screening arm of the

study. At baseline, men received a prostate-specific antigen (PSA) test and digital rectal exam (DRE) for prostate cancer screening; then received both screenings annuals for the subsequent 3 or 5 years. All participants were asked to complete annual questionnaires regarding cancer diagnoses during the previous year.

Statistical Analysis

Cox proportional hazards regression, with age as underlying time metric, was used to estimate relative risks (RR) and 95% confidence intervals for prostate cancer. The models were adjusted for race, study center (multi-center study), family history of prostate cancer, body mass index, smoking status, physical activity level, total energy intake, supplemental vitamin E intake, history of diabetes, lycopene intake, aspirin use and total number of exams during follow-up.

Data Collection Summary:

Timing of Measurements

At baseline and annually, all participants received a prostate-specific antigen (PSA) test and digital rectal exam (DRE) for prostate cancer screening, complete annual questionnaires regarding cancer diagnoses during previous year.

Just at baseline, participants completed a general risk factor questionnaire and self-administered food frequency questionnaire (FFQ) of consumption and portion size of 137 foods during previous year. The FFQ asked detailed information about the meat-cooking methods and doneness level.

Dependent Variables

- Prostate cancer: pathologically confirmed as incident (diagnosed after first year of follow-up) or advanced prostate cancer
- Daily intake of meat mutagens: developed a database to estimate daily intake of meat mutagens

Description of Actual Data Sample:

Initial N: 38,352 (all participants were male)

Attrition (final N): 29,361

Age: Aged between 55-74 years at entry

Ethnicity: Non-Hispanic white (90.7%), Asian/Pacific Islander (4%), Black (3.3%), Hispanic/American Indian/Alaskan (1.9%)

Location: Multi-site study (Birmingham, AL; Denver, CO; Detroit, MI; Honolulu, HI; Marshfield, WI; Minneapolis, MN; Pittsburgh, PA; Salt Lake City, UT; St. Louis, MO; and Washington, DC)

Summary of Results:

Key Findings

- During follow-up, a total of 1,338 prostate cancer cases were diagnosed, of which 868 were incident cases and 520 were advanced cases
- 9% of the participants died or were lost during follow-up
- Men in the highest quintile for red meat intake were more likely to b e younger, obese, have higher total energy intake, consume more lycopene and less likely to use vitamin E supplements
- Those who ate the most red meat were also less likely to exercise, eat fruits and vegetables and more likely to be current smokers
- There was no association between red or white meat consumption, cooking method or doneness of meats and the risk of prostate cancer
- Processed meat intake was not associated with overall prostate cancer risk or incident disease
- The risk of advanced prostate cancer was highest in those in the highest four quintiles of consumption, although there was no evidence of a dose-response trend
- Consumption of >10 g/d of very well done meat was associated with a 42% increased risk for prostate cancer and a 69% increased risk for incident disease

Author Conclusion:

The authors concluded that a high intake of very well done meat and a high intake of 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP) were both positively associated with prostate cancer risk.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	Yes
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	No
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	Yes
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes

7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes